

PGPB,USPT; PLUR=YES; OP=ADJ

L8 L6 same (alloimmun\$ or immun\$)same(inhibit\$ or suppress\$ or prevent\$ or block\$) 20 L8

L7 L6 same (alloimmun\$ or immun\$)same(inhibit\$ or suppress\$ or prevent\$ or block\$) 20 L7

L6 (olgiomer\$ or trimer\$ or multimer\$ or dimer\$)same(Cd40L or cd40 adj ligand or gp39 or cd154) 175 L6

L5 (18 kd\$ or'18 kd\$') and (Cd40L or cd40 adj ligand or gp39 or cd154) 0 L5

L4 (18 kd\$ or'18 kd\$') same (Cd40L or cd40 adj ligand or gp39 or cd154) 0 L4

L3 (18kd\$ or'18kd\$') same (Cd40L or cd40 adj ligand or gp39 or cd154) 0 L3

L2 L1 and (Cd40L or cd40 adj ligand or gp39 or cd154) 0 L2

L1 lazarus.in.

09/579548

Search Results - Record(s) 1 through 10 of 20 returned.

☐ 1. Document ID: US 20040047873 A1

Using default format because multiple data bases are involved.

L8: Entry 1 of 20

File: PGPB

Mar 11, 2004

PGPUB-DOCUMENT-NUMBER: 20040047873

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040047873 A1

TITLE: Materials and methods relating to the increase in protein activity

PUBLICATION-DATE: March 11, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Al- Shamkhani, Aymen	Southampton		GB	
Glennie, Martin	Southampton		GB	

US-CL-CURRENT: 424/185.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWMC	Draw D
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☐ 2. Document ID: US 20040002060 A1

L8: Entry 2 of 20

File: PGPB

Jan 1, 2004

PGPUB-DOCUMENT-NUMBER: 20040002060

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040002060 A1

TITLE: Fiber shaft modifications for efficient targeting

PUBLICATION-DATE: January 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kaleko, Michael	Rockville	MD	US	
Nemerow, Glen R.	Encinitas	CA	US	
Smith, Theodore	Ijamsville	MD	US	
Stevenson, Susan C.	Frederick	MD	US	

US-CL-CURRENT: 435/5; 435/235.1, 435/320.1, 435/325, 435/456, 435/69.3, 530/350, 536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWMC	Draw D
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☐ 3. Document ID: US 20030219875 A1

L8: Entry 3 of 20

File: PGPB

Nov 27, 2003

PGPUB-DOCUMENT-NUMBER: 20030219875
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030219875 A1

TITLE: Albumin fusion proteins

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rosen, Craig A.	Laytonsville	MD	US	
Haseltine, William A.	Washington	DC	US	

US-CL-CURRENT: 435/69.7; 435/320.1, 435/325, 514/12, 530/362, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw. De
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☐ 4. Document ID: US 20030215948 A1

L8: Entry 4 of 20

File: PGPB

Nov 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030215948
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030215948 A1

TITLE: Fiber shaft modifications for efficient targeting

PUBLICATION-DATE: November 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kaleko, Michael	Rockville	MD	US	
Nemerow, Glen R.	Encintas	CA	US	
Smith, Theodore	Ijamsville	MD	US	
Stevenson, Susan C.	Frederick	MD	US	

US-CL-CURRENT: 435/456; 435/235.1, 435/320.1, 435/370

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw. De
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☐ 5. Document ID: US 20030143196 A1

L8: Entry 5 of 20

File: PGPB

Jul 31, 2003

PGPUB-DOCUMENT-NUMBER: 20030143196
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030143196 A1

TITLE: Canine IL-13 nucleic acid molecules and uses thereof

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sim, Gek-Kee	Fort Collins	CO	US	
Yang, Shumin	Palo Alto	CA	US	
Dreitz, Matthew J.	Fort Collins	CO	US	
Wonderling, Ramani S.	Fort Collins	CO	US	

US-CL-CURRENT: 424/85.2; 435/320.1, 435/325, 435/350, 435/69.52, 530/350, 530/351, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. Des
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☐ 6. Document ID: US 20030109440 A1

L8: Entry 6 of 20

File: PGPB

Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109440

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109440 A1

TITLE: GRB7: novel regulator of lymphocyte signaling

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Chu, Peter	San Francisco	CA	US	
Li, Congfen	Davis	CA	US	
Liao, X. Charlene	Palo Alto	CA	US	
Masuda, Esteban	Menlo Park	CA	US	
Pardo, Jorge	San Francisco	CA	US	
Zhao, Haoran	Foster City	CA	US	

US-CL-CURRENT: 514/12; 435/6, 435/7.1, 435/7.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. Des
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☐ 7. Document ID: US 20030099609 A1

L8: Entry 7 of 20

File: PGPB

May 29, 2003

PGPUB-DOCUMENT-NUMBER: 20030099609

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030099609 A1

TITLE: Canine IL-4 nucleic acid molecules and uses thereof

PUBLICATION-DATE: May 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sim, Gek-Kee	Fort Collins	CO	US	
Yang, Shumin	Fort Collins	CO	US	
Dreitz, Matthew J.	Fort Collins	CO	US	
Wonderling, Ramani S.	Fort Collins	CO	US	

US-CL-CURRENT: 424/85.2; 435/320.1, 435/350, 435/69.52, 530/351, 536/23.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 8. Document ID: US 20030077667 A1

L8: Entry 8 of 20

File: PGPB

Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077667

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030077667 A1

TITLE: Methods and compounds for disruption of CD40R/CD40L signaling in the treatment of alzheimer's disease

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Tan, Jun	Tampa	FL	US	
Town, Terrence C.	Tampa	FL	US	
Mullan, Michael	Tampa	FL	US	

US-CL-CURRENT: 435/7.2; 424/144.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 9. Document ID: US 20030022196 A1

L8: Entry 9 of 20

File: PGPB

Jan 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030022196

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030022196 A1

TITLE: Methods and compositions for screening for altered cellular phenotypes

PUBLICATION-DATE: January 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
------	------	-------	---------	---------

Lorens, James	Portola Valley	CA	US
Kinsella, Todd M.	Fayetteville	CA	US
Masuda, Esteban	Menlo Park	CA	US
Hitoshi, Yasumichi	Mountain view	CA	US
Liao, X. Charlene	Palo Alto	CA	US
Pearsall, Denise	Belmont	CA	US
Friera, Annabelle	South San Francisco	CA	US
Chu, Peter	San Francisco	CA	US

US-CL-CURRENT: 435/6; 435/325, 435/455, 435/7.21

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 10. Document ID: US 20030021808 A1

L8: Entry 10 of 20

File: PGPB

Jan 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030021808

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030021808 A1

TITLE: Cd40 ligand adjuvant for respiratory syncytial virus

PUBLICATION-DATE: January 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Tripp, Ralph A	Decatur	GA	US	
Anderson, Larry J	Atlanta	GA	US	
Brown, Michael P	St Georges, South Autralia		AU	

US-CL-CURRENT: 424/211.1; 424/199.1, 424/204.1, 424/278.1, 435/91.1, 536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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ALLOIMMUNE-MEDIATED	1
ALLOIMMUNISATION	1
ALLOIMMUNISED	4

ALLOIMMUNITY	22
ALLOIMMUNIZATION	157
ALLOIMMUNIZATIONS	5
ALLOIMMUNIZATION-INDUCED	2
"ALLOIMMUNIZATION[28]"	1
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L8: Entry 11 of 20

File: PGPB

Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013107

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030013107 A1

TITLE: Alpha 2 integrin: modulators of lymphocyte activation

PUBLICATION-DATE: January 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Chu, Peter	San Francisco	CA	US	
Li, Congfen	Davis	CA	US	
Liao, X. Charlene	Palo Alto	CA	US	
Pardo, Jorge	San Francisco	CA	US	

US-CL-CURRENT: 435/6; 435/372, 435/7.21

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWMC	Draw. De
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☐ 12. Document ID: US 20020168359 A1

L8: Entry 12 of 20

File: PGPB

Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168359

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168359 A1

TITLE: Human tumor necrosis factor receptor TR9

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ni, Jian	Germantown	MD	US	
Yu, Guo-Liang	Berkeley	CA	US	
Fan, Ping	Potomac	MD	US	
Gentz, Reiner L.	Rockville	MD	US	

US-CL-CURRENT: 424/139.1; 435/320.1, 435/325, 435/69.1, 530/350, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWMC	Draw. De
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☐ 13. Document ID: US 20020155512 A1

L8: Entry 13 of 20

File: PGPB

Oct 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020155512

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020155512 A1

TITLE: EDG: modulators of lymphocyte activation and migration

PUBLICATION-DATE: October 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Liao, X. Charlene	Palo Alto	CA	US	
Masuda, Esteban	Menlo Park	CA	US	
Chu, Peter	San Francisco	CA	US	
Pardo, Jorge	San Francisco	CA	US	
Li, Congfen	Davis	CA	US	
Zhao, Haoran	Foster City	CA	US	
Jiang, Ying-Ping	Piedmont	CA	US	

US-CL-CURRENT: [435/7.21](#); [435/6](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draws
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☐ 14. Document ID: US 20020146747 A1

L8: Entry 14 of 20

File: PGPB

Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146747

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020146747 A1

TITLE: TRAC1: modulators of lymphocyte activation

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Masuda, Esteban	Menlo Park	CA	US	
Liao, X. Charlene	Palo Alto	CA	US	
Zhao, Haoran	Foster City	CA	US	
Chu, Peter	San Francisco	CA	US	
Pardo, Jorge	San Francisco	CA	US	

US-CL-CURRENT: [435/7.21](#); [435/18](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draws
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☐ 15. Document ID: US 20020142325 A1

L8: Entry 15 of 20

File: PGPB

Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142325

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020142325 A1

TITLE: PAK 2: modulators of lymphocyte activation

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Liao, X. Charlene	Palo Alto	CA	US	
Chu, Peter	San Francisco	CA	US	
Pardo, Jorge	San Francisco	CA	US	
Li, Congfen	Davis	CA	US	
Zhao, Haoran	Foster City	CA	US	
Wu, Jun	Sunnyvale	CA	US	

US-CL-CURRENT: 435/6; 435/7.21

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 16. Document ID: US 20020022017 A1

L8: Entry 16 of 20

File: PGPB

Feb 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020022017

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020022017 A1

TITLE: Regulation of systemic immune responses utilizing soluble CD40

PUBLICATION-DATE: February 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yu, Hua	Tampa	FL	US	

US-CL-CURRENT: 424/93.21; 424/85.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. De
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☐ 17. Document ID: US 6673908 B1

L8: Entry 17 of 20

File: USPT

Jan 6, 2004

US-PAT-NO: 6673908
DOCUMENT-IDENTIFIER: US 6673908 B1

TITLE: Tumor necrosis factor receptor 2

DATE-ISSUED: January 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stanton, Jr.; Vincent P.	Belmont	MA		

US-CL-CURRENT: 536/22.1; 435/6, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.31,
536/24.33

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KWIC	Draw D
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☐ 18. Document ID: US 6562811 B1

L8: Entry 18 of 20

File: USPT

May 13, 2003

US-PAT-NO: 6562811
DOCUMENT-IDENTIFIER: US 6562811 B1

TITLE: Pyridine derivatives

DATE-ISSUED: May 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Murata; Toshiki	Nara-ken			JP
Umeda; Masaomi	Nara-ken			JP
Sakakibara; Sachiko	Nara-ken			JP
Yoshino; Takashi	Nara			JP
Sato; Hiroki	Nara			JP
Masuda; Tsutomu	Nara-ken			JP
Koriyama; Yuji	Nara			JP
Shimada; Mitsuyuki	Meerbusch			DE
Shintani; Takuya	Kyoto-fu			JP
Kadono; Hiroshi	Nishinomiya			JP
Lowinger; Timothy B.	Nishinomiya			JP
Ziegelbauer; Karl B.	Haan			DE
Fuchikami; Kinji	Kyoto-fu			JP
Komura; Hiroshi	Nara			JP

US-CL-CURRENT: 514/222.5; 514/226.5, 514/230.5, 514/234.2, 514/248, 514/300,
514/303, 544/10, 544/117, 544/127, 544/2, 544/279, 544/362, 544/48, 544/91,
546/119, 546/122, 546/123

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KWIC	Draw D
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☐ 19. Document ID: US 6482411 B1

L8: Entry 19 of 20

File: USPT

Nov 19, 2002

US-PAT-NO: 6482411

DOCUMENT-IDENTIFIER: US 6482411 B1

**** See image for Certificate of Correction ****

TITLE: Methods of reducing bone loss with CD40 ligand

DATE-ISSUED: November 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ahuja; Seema A.	San Antonio	TX		
Bonewald; Lynda F.	San Antonio	TX		

US-CL-CURRENT: 424/185.1; 424/178.1, 424/184.1, 424/192.1, 424/85.1, 514/12, 514/2,
514/8, 514/885, 530/350, 530/351

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Claims	KWIC	Drawings
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☐ 20. Document ID: US 6358508 B1

L8: Entry 20 of 20

File: USPT

Mar 19, 2002

US-PAT-NO: 6358508

DOCUMENT-IDENTIFIER: US 6358508 B1

TITLE: Antibodies to human tumor necrosis factor receptor TR9

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ni; Jian	Rockville	MD		
Yu; Guo-Liang	Berkeley	CA		
Fan; Ping	Gaithersburg	MD		
Gentz; Reiner L.	Rockville	MD		

US-CL-CURRENT: 424/139.1;

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E4	149	AU=LAZARUS A
E5	73	AU=LAZARUS A A
E6	1	AU=LAZARUS A B
E7	4	AU=LAZARUS A E
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E9	5	AU=LAZARUS A L
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E19	5	AU=LAZARUS ADAM B
E20	48	AU=LAZARUS ALAN H
E21	2	AU=LAZARUS AMBER D
E22	3	AU=LAZARUS AMY
E23	1	AU=LAZARUS ANGELINE
E24	8	AU=LAZARUS ANGELINE A

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E3 0 *AU=LAZARUS ALAN ?
 E4 48 AU=LAZARUS ALAN H
 E5 2 AU=LAZARUS AMBER D
 E6 3 AU=LAZARUS AMY
 E7 1 AU=LAZARUS ANGELINE
 E8 8 AU=LAZARUS ANGELINE A
 E9 1 AU=LAZARUS ARMAND
 E10 11 AU=LAZARUS ARNAUD
 E11 6 AU=LAZARUS ARNOLD A
 E12 7 AU=LAZARUS ARTHUR

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S1 48 AU='LAZARUS ALAN H'
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 48 S1
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 20434 CD40
 375499 LIGAND
 9410 CD40 (W) LIGAND
 2215 CD154

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0013150295 BIOSIS NO.: 200100322134
 Mice lacking CD40 or **CD154** (**CD40L**) exhibit distinct abnormalities in haemostasis
 AUTHOR: Crow Andrew R (Reprint); Freedman John (Reprint); Mody Meera (Reprint); Rand Margaret L; **Lazarus Alan H** (Reprint
 AUTHOR ADDRESS: Transfusion Medicine Research and the Department of Laboratory Medicine and Pathobiology, St. Michael's Hospital, Toronto, Canada**Canada
 JOURNAL: Blood 96 (11 Part 1): p622a November 16, 2000 2000
 MEDIUM: print
 CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201
 SPONSOR: American Society of Hematology
 ISSN: 0006-4971
 DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
 RECORD TYPE: Abstract
 LANGUAGE: English

ABSTRACT: The co-stimulatory molecule CD40 and its natural ligand **CD154** (**CD40L**) are expressed on antigen presenting cells and activated T cells, respectively, and play a major role in immune responses. *****CD154***** is also expressed on activated platelets and, through its potential interaction with CD40 on endothelial cells and macrophages, has been hypothesised to be involved in inflammatory responses, including the release of tissue factor and proinflammatory cytokines, potentially leading to thrombus formation. We wished to elucidate if the absence of CD40 and **CD154** affects haemostatic regulation. Here, we demonstrate that C57BL/6 mice genetically lacking CD40 (CD40-/-) or **CD154** (**CD154**-/-) have significantly prolonged bleeding times compared with wild-type mice and control beta-2 microglobulin deficient (beta2M-/-) mice (P=0.001, P=0.03, respectively; n=8). To determine if a 'platelet abnormality' is responsible for this altered haemostasis, we examined both platelet activation and platelet function in CD40-/- and *****CD154***** -/- mice. In comparison with wild-type C57BL/6 mice and control beta2M-/- deficient mice, platelet activation in CD40-/- and **CD154**-/- mice was found to be normal in response to

thrombin and ADP, as analysed by flow cytometry (n=8). Platelet function was analysed at high shear stress using a platelet function analyser (PFA-100), which measures closure time (the time for platelets in whole blood to occlude a 150 µm diameter hole in a collagen/epinephrine coated membrane). Platelet plug formation was abnormal (i.e. increased closure time) in the ***CD154*** -/- mice (P=0.001; n=5), and normal in the CD40-/- mice (n=5). These data indicate that both CD40 and CD154 expression are required for normal haemostasis and that ***CD154*** -/- mice possess defects in platelet function. CD40-/- mice have normal platelet function, and the etiology of the prolonged bleeding time remains to be determined.

? s (cd40(W)ligand or cd40L or gp39 or cd154) (20n) (18(W) (kd?)

>>>Unmatched parentheses

? s (cd40(W)ligand or cd40L or gp39 or cd154) (20n) (18(W)kd?)

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20434 CD40
375499 LIGAND
9410 CD40(W)LIGAND
5074 CD40L
615 GP39
2215 CD154
1219157 18
414249 KD?

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S3 15 (CD40(W)LIGAND OR CD40L OR GP39 OR CD154) (20N) (18(W)KD?)

? rd s3

...completed examining records

S4 5 RD S3 (unique items)

? t s4/7/all

4/7/1 (Item 1 from file: 5)

DIALOG(R)File 5:BIOSIS Previews(R)

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0013237105 BIOSIS NO.: 200100408944

The inflammatory action of CD40 ligand (CD154) expressed on activated human platelets is temporally limited by coexpressed CD40

AUTHOR: Henn Volker; Steinbach Sabine; Buechner Kerstin; Presek Peter; Krocze Richard A (Reprint)

AUTHOR ADDRESS: Molecular Immunology, Robert Koch-Institute, Nordufer 20, 13353, Berlin, Germany**Germany

JOURNAL: Blood 98 (4): p1047-1054 August 15, 2001 2001

MEDIUM: print

ISSN: 0006-4971

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RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Recently, we have demonstrated that human platelets carry preformed CD40 ligand (CD154) molecules, which rapidly appear on the platelet surface following stimulation by thrombin. Once on the surface, platelet CD154 induces an inflammatory reaction of CD40-bearing endothelial cells. This study shows that strong platelet agonists other than thrombin also lead to the expression of CD154 on the platelet surface. At the same time, several lines of evidence are presented that together indicate that thrombotic events in the vasculature are generally accompanied by activation of the inflammatory potential of platelet CD154. This study also reports the constitutive expression of CD40, the receptor for CD154, on platelets. The binding of CD154 to coexpressed CD40 in the platelet aggregate leads within minutes to hours to the cleavage of membrane-bound surface CD154 and the release of an ***18*** - ***kd*** soluble form of the molecule. Soluble ***CD154*** (sCD154), in contrast to transmembrane CD154, can no longer induce an inflammatory reaction of endothelial cells. These findings indicate that the interaction of platelet CD154 with CD40 on neighboring cells is temporally limited to prevent an uncontrolled inflammation at the site of

thrombus formation. Thus, similar to the very tight regulation of the CD154-CD40 interaction in the immune system, an effective mechanism controls the inflammatory potential of platelet CD154 in the vascular system.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0012185463 BIOSIS NO.: 199900445123

Inhibition of a secondary human alloimmune response via the soluble active component of CD154 (CD40L) in severe combined immune-deficient mice engrafted with human lymphocytes

AUTHOR: Lazarus A H (Reprint); Crow A R; Freedman J; Blanchette V; Hannach B

AUTHOR ADDRESS: Department of Immunohaematology, St. Michael's Hospital, 30 Bond Street, Toronto, ON, M5B 1W8, Canada**Canada

JOURNAL: Transfusion (Bethesda) 39 (8): p818-823 Aug., 1999 1999

MEDIUM: print

ISSN: 0041-1132

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: BACKGROUND: Alloimmunization requires a process known as co-stimulation. An important co-stimulatory pathway for most immune responses is mediated by the interaction of CD40 on antigen-presenting cells with CD154 (CD40L) on host T cells. Blockade of this co-stimulatory pathway simultaneous with exposure to challenge with HLA-incompatible cells is hypothesized to inhibit alloimmunization. STUDY DESIGN AND METHODS: Severe combined immune-deficient (SCID) mice were reconstituted with human peripheral blood lymphocytes (Hu-PBL-SCID mice) from a subject primed to HLA antigens and challenged with HLA-incompatible lymphocytes. Mice were challenged in the presence or absence of an **18-kDa** soluble recombinant active form of human **CD154 (18-kDa ***CD154***)**. Human IgG production, alloimmunization, and in vitro T-cell responsiveness were assessed. RESULTS: There was no significant effect of **18-kDa CD154** on human IgG levels in these mice, but it inhibited the development of HLA-specific alloantibody in this model to five subsequent untreated white cell challenges. In vitro T-cell proliferation in a mixed lymphocyte culture was also prevented by *****18*** - ***kDa*** ***CD154*****. CONCLUSION: The recombinant protein **18-kDa CD154** inhibited the ability of the Hu-PBL-SCID mice to mount a secondary immune response to allostimulation. This implies that transfusion-induced alloimmunization utilizes CD40-CD154 co-stimulation and that blockade of this pathway can inhibit T-cell function and interfere with the development of alloimmunization.

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0011386663 BIOSIS NO.: 199800180910

Regulation of cytoplasmic, surface and soluble forms of CD40 ligand in mouse B cells

AUTHOR: Wykes Michelle; Poudrier Johanne; Lindstedt Ragnar; Gray David (Reprint)

AUTHOR ADDRESS: Dep. Immunol., Imperial Coll. Sch. Med., Hammersmith Hosp., Du Cane Rd., London W12 0NN, UK**UK

JOURNAL: European Journal of Immunology 28 (2): p548-559 Feb., 1998 1998

MEDIUM: print

ISSN: 0014-2980

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CD40 and CD40 ligand (CD40L) form one of most important receptor-ligand pairs that dock during T-B cell interactions as part of T-dependent antibody responses. It has been reported that among other cell types, B cells can express CD40L. Here we show that a large proportion of mouse B cells express CD40L in their cytoplasm, but not on the surface and that this is readily released as a soluble molecule. Thus, in their resting state up to 50% of mouse B cells express CD40L within their cytoplasm and both the proportion of cells expressing and the amount of CD40L is increased by signaling through immunoglobulin (Ig) or CD38. In contrast, T cell-derived signals such as CD40L (anti-CD40) or Th2-type cytokines cause a decrease in CD40L expression that is related to a release of a soluble form of the molecule from the cell. Supernatants from B cells activated with anti-Ig and anti-CD40 contain CD40L in a variety of forms (18 kDa, 33 kDa and 66 kDa) that are readily detectable by immunoprecipitation with CD40-Fc γ fusion protein (CD40-Ig) followed by Western blotting with anti-CD40L antibody (MR1). The 33-kDa species is distinct from the 39-kDa membrane-bound molecule found in activated T cells or in resting B cells and appears to be a novel soluble form of CD40L. Inhibition of T cell-independent in vitro stimulation of B cells with CD40-Ig or anti-CD40L suggests that the B cell-derived soluble CD40L or CD40L expressed on the B cell surface can play a positive role in B cell proliferation.

4/7/4 (Item 4 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
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0010725643 BIOSIS NO.: 199799359703
Heteromultimeric complexes of CD40 ligand are present on the cell surface of human T lymphocytes
AUTHOR: Hsu Yen-Ming (Reprint); Lucci Jodie; Su Lihe; Ehrenfels Barbara; Garber Ellen; Thomas David
AUTHOR ADDRESS: Dep. Protein Eng., Biogen Inc., 14 Cambridge Center, Cambridge, MA 02142, USA**USA
JOURNAL: Journal of Biological Chemistry 272 (2): p911-915 1997 1997
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CD40 ligand (CD40L), a 33-kDa type II membrane glycoprotein expressed primarily on activated CD4⁺ T lymphocytes, is responsible for the helper function of T cells on resting B cells in a non-antigen-dependent, non-major histocompatibility complex-restricted fashion. Interaction of CD40L with its receptor CD40 induces proliferation of and isotype switching in B lymphocytes. Recently we solved the x-ray structure of recombinant soluble CD40L and showed that, similar to other members of the tumor necrosis factor family, CD40L indeed exists as a trimer. We now report that, under normal physiological conditions, CD40L molecules exist as heteromultimeric complexes. These CD40L complexes, made of the full length and smaller fragments of CD40L, are present on the cell surface of T lymphocytes and are capable of interacting with CD40 molecule. A prominent fragment with a mass of 31 kDa accounts for as much as half of the CD40L on the surface of Jurkat cells. Nterminal sequence data revealed that this fragment lacks the cytoplasmic tail. A minor ***18*** - ***kDa*** fragment of ***CD40L***

was also characterized which lacks the cytoplasmic tail, transmembrane

region, and stalk region of the extracellular domain. The presence of CD40L heteromultimeric variants implies an additional regulation of the functional activity of this ligand complex.

4/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS Previews(R)
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0009799738 BIOSIS NO.: 199598267571
Recombinant soluble trimeric CD40 ligand is biologically active
AUTHOR: Mazzei Gonzalo J (Reprint); Edgerton Michael D; Losberger
Christophe; Lecoanet-Henchoz Sybille; Graber Pierre; Durandy Anne;
Gauchat Jean-Francois; Bernard Alain; Allet Bernard; Bonnefoy Jean-Yves
AUTHOR ADDRESS: Glaxo Inst. Mol. Biol., 14 Chemin des Aulx, 1228 Plan les
Ouates, Geneva, Switzerland**Switzerland
JOURNAL: Journal of Biological Chemistry 270 (13): p7025-7028 1995 1995
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CD40 ligand (CD40L) is expressed on the surface of activated CD4+ T cells, basophils, and mast cells. Binding of CD40L to its receptor, CD40, on the surface of B cells stimulates B cell proliferation, adhesion and differentiation. A preparation of soluble, recombinant CD40L (Tyr-45 to Leu-261), containing the full-length 29-kDa protein and two smaller fragments of 18 and 14 kDa, has been shown to induce differentiation of B cells derived either from normal donors or from patients with X-linked hyper-IgM syndrome (Durandy, A., Schiff, C., Bonnefoy, J.-Y., Forveille, M., Rousset, F., Mazzei, G., Milili, M., and Fischer, A. (1993) Eur. J. Immunol. 23, 2294-2299). We have now purified each of these fragments to homogeneity and show that only the 18-kDa fragment (identified as Glu-108 to Leu-261) is biologically active. When expressed in recombinant form, the 18-kDa protein exhibited full activity in B cell proliferation and differentiation assays, was able to rescue of B cells from apoptosis, and bound soluble CD40. Sucrose gradient sedimentation shows that the 18-kDa protein sediments as an apparent homotrimer, a result consistent with the proposed trimeric structure of ***CD40L***. This demonstrates that a soluble CD40L can stimulate CD40 in a manner indistinguishable from the membrane-bound form of the protein.

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